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CLAIMS

1. Use of an antagonist of the CB1 receptor in the manufacture of a composition for the treatment of hepatic diseases which result in hepatic fibrosis.

2. Use according to claim 1 wherein the antagonist of the CB1 receptor is a specific antagonist of the CB1 receptor.

3. Use according to claims 1 to 2 wherein the hepatic disease is alcoholic liver cirrhosis.

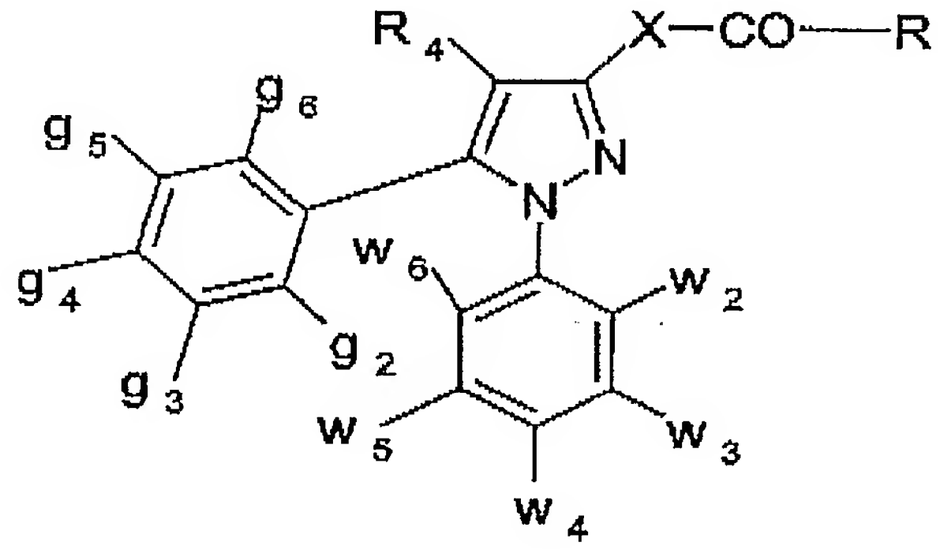
4. Use according to claims 1 to 2 wherein the hepatic disease is chronic viral hepatitis.

5. Use according to claims 1 to 2 wherein the hepatic disease is non-alcoholic steatohepatitis.

6. Use according to claims 1 to 2 wherein the hepatic disease is primary liver cancer.

7. Use according to claims 1 to 6 wherein the antagonist is a compound of the formula II or one of its pharmaceutically acceptable salt, in which g_2, g_3, g_4, g_5 and g_6 and w_2, w_3, w_4, w_5 and w_6 are identical or different and are independently hydrogen, a chlorine or bromine atom, a (C_1-C_3) alkyl, a (C_1-C_3) alkoxy, a trifluoromethyl or a nitro group and g_4 is optionally a phenyl group; R_4 is hydrogen or a (C_1-C_3) alkyl; X is either a direct bond or a group $-(CH_2)_x-N(R_3)-$, in which R_3 is hydrogen or a (C_1-C_3) alkyl and x is zero or one; R is: a group $-NR_1R_2$ in which R_1 and R_2 are independently a (C_1 -C_6)-alkyl; an non-aromatic (C_3-C_{15}) carbocyclic radical which is optionally substituted, said substituent(s) being other than a substituted carbonyl; an amino (C_1-C_4) alkyl group in which the amino is optionally disubstituted by a (C_1-C_3) alkyl; a cycloalkyl (C_1-C_3) alkyl in which the cycloalkyl is C_3-C_{12}; a phenyl which is unsubstituted or monosubstituted or polysubstituted by a halogen, by a (C_1-C_5) alkyl or by a (C_1-C_5) alkoxy; a phenyl (C_1-C_3) alkyl; a diphenyl (C_1-C_3) alkyl; a naphthyl; an anthracenyl; a saturated 5- to 8-membered heterocyclic radical which is unsubstituted or substituted by a (C_1-C_3) alkyl, by a hydroxyl or by a benzyl; a 1-adamantylmethyl; an aromatic heterocycle which is unsubstituted or monosubstituted or polysubstituted by a halogen, by a (C_1-C_5) alkyl or by a (C_1-C_5) alkoxy; a (C_1-C_3) alkyl which is substituted by an aromatic heterocycle which is unsubstituted or monosubstituted or polysubstituted by a halogen, by a (C_1-C_5) alkyl or by a (C_1-C_5) alkoxy; or else R_1 is hydrogen and R_2 is as defined above; or else R_1 and R_2 form a saturated 5- to 8-membered heterocyclic radical with the nitrogen atom to which they are bonded, said heterocyclic radical being other

than morpholine when w_2, w_3, w_4, w_5, w_6, g_2, g_3, g_4, g_5 and g_6 are all hydrogen; a group R_2 as defined above when X is $-(CH_2)_x N(R_3)-$; a group R_5 when X is a direct bond, R_5 being a (C_1-C_3) alkyl; a (C_3-C_{12}) cycloalkyl which is unsubstituted or substituted by a (C_1-C_5) alkyl; a phenyl (C_1-C_3) alkyl which is unsubstituted or substituted by a halogen or by a (C_1-C_5) alkyl; a cycloalkyl (C_1-C_3) alkyl in which the cycloalkyl is C_3-C_{12} and is unsubstituted or substituted by a (C_1 -C_5) alkyl; or a 2-norbornylmethyl.



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8. Use according to claims 1 to 6 wherein the antagonist is N-piperidono-3-pyrazolecarboxamide or one of its pharmaceutically acceptable salt.

9. Use according to claims 1 to 6 wherein the antagonist is N-piperidino-5-(4-bromophenyl)-1-(2,4-dichlorophenyl)-4-ethylpyrazole-3-carboxamide or one of its pharmaceutically acceptable salt.

10. Use according to claims 1 to 6 wherein the antagonist is N-piperidino-5-(4-chlorophenyl)-1-(2, 4-dichlorophenyl)-4-methylpyrazole-3- carboxamide or one of its pharmaceutically acceptable salt.

11. Use according to any of the preceding claims wherein the CB1 receptor is selected from the group consisting of:

a) a protein having an amino acid sequence comprising SEQ ID NO:1 or a portion of SEQ ID NO:1, having the biological function of a G protein-coupled cellular receptor, capable of binding THC and transducing a cellular signal;

b) a protein having an amino acid sequence comprising SEQ ID NO:2 or a portion of SEQ ID NO:2, having the biological function of a G protein-coupled cellular receptor, capable of binding THC and transducing a cellular signal;

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c) an allele of the protein having the amino acid sequence of SEQ ID NO:1 or SEQ ID NO:2, having the biological function of a G protein-coupled cellular receptor, capable of binding THC and transducing a cellular signal;

d) a protein having the amino acid sequence of SEQ ID NO:1 with a Phenylalanine to Leucine substitution at position 200; and/or an Isoleucine to Valine substitution at position 216; and/or a Valine to Alanine substitution at position 246;

e) a protein having the amino acid sequence of SEQ ID NO:2 with a Phenylalanine to Leucine substitution at position 139; and/or an Isoleucine to Valine substitution at position 155; and/or a Valine to Alanine substitution at position 185; and

f) a protein comprising the amino acid sequences of SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8 and SEQ ID NO:9 or amino acid sequences 80 % homologous to these, said protein having the biological function of a G protein-coupled cellular receptor, capable of binding THC and transducing a cellular signal.

12. Use according to claims 1 to 10 wherein the CB1 receptor is a protein having a homology at the amino acid level with SEQ ID NO:1 of at least 45%, having the biological function of a G protein-coupled cellular receptor, capable of binding THC and transducing a cellular signal.

13. Use according to the preceding claim wherein the homology is at least 60%, preferably 70 %, more preferably 80 %, even more preferably 90 % and more preferably 95 %.

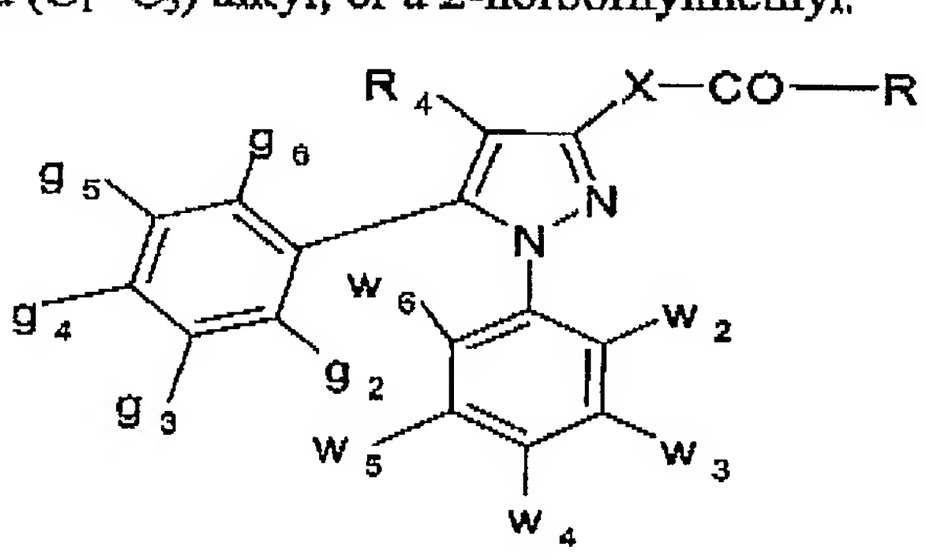
14. Use according to any of the preceding claims wherein the daily dosage of CB1 receptor antagonist is from 0.01mg to 500mg, preferably from 1 mg to 100 mg.

15. Use of a nucleic acid sequence coding for a protein comprising SEQ ID NO:1 or SEQ ID NO:2 or a portion of SEQ ID NO:1 or a portion of SEQ ID NO:2, for the preparation of a composition for the treatment of hepatic diseases which result in hepatic fibrosis, by the downregulation or suppression of the CB1 receptor.

16. A method of treatment of hepatic diseases which result in hepatic fibrosis in a mammal comprising the administration of a therapeutically effective amount of at least one CB1 receptor antagonist to a mammal in need thereof.

17. A method of treatment of hepatic diseases according to claim 16 wherein the CB1 receptor antagonist is a compound of the formula II or one of its pharmaceutically

acceptable salt, in which g_2, g_3, g_4, g_5 and g_6 and w_2, w_3, w_4, w_5 and w_6 are identical or different and are independently hydrogen, a chlorine or bromine atom, a (C_1-C_3) alkyl, a (C_1-C_5) alkoxy, a trifluoromethyl or a nitro group and g_4 is optionally a phenyl group; R_4 is hydrogen or a (C_1-C_3) alkyl; X is either a direct bond or a group -$(CH_2)_x$ -$N(R_3)$-, in which R_3 is hydrogen or a (C_1-C_3) alkyl and x is zero or one; R is: a group -NR_1 R_2 in which R_1 and R_2 are independently a (C_1 -C_6)-alkyl; an non-aromatic (C_3-C_{15}) carbocyclic radical which is optionally substituted, said substituent(s) being other than a substituted carbonyl; an amino (C_1-C_4) alkyl group in which the amino is optionally disubstituted by a (C_1-C_3) alkyl; a cycloalkyl (C_1-C_3) alkyl in which the cycloalkyl is C_3-C_{12}; a phenyl which is unsubstituted or monosubstituted or polysubstituted by a halogen, by a (C_1-C_5) alkyl or by a (C_1-C_5) alkoxy; a phenyl (C_1-C_3) alkyl; a diphenyl (C_1-C_3) alkyl; a naphthyl; an anthracenyl; a saturated 5- to 8-membered heterocyclic radical which is unsubstituted or substituted by a (C_1-C_3) alkyl, by a hydroxyl or by a benzyl; a 1-adamantylmethyl; an aromatic heterocycle which is unsubstituted or monosubstituted or polysubstituted by a halogen, by a (C_1-C_5) alkyl or by a (C_1-C_5) alkoxy; a (C_1-C_3) alkyl which is substituted by an aromatic heterocycle which is unsubstituted or monosubstituted or polysubstituted by a halogen, by a (C_1-C_5) alkyl or by a (C_1-C_5) alkoxy; or else R_1 is hydrogen and R_2 is as defined above; or else R_1 and R_2 form a saturated 5- to 8-membered heterocyclic radical with the nitrogen atom to which they are bonded, said heterocyclic radical being other than morpholine when w_2, w_3, w_4, w_5, w_6, g_2, g_3, g_4, g_5 and g_6 are all hydrogen; a group R_2 as defined above when X is -$(CH_2)_x$ $N(R_3)$-; a group R_5 when X is a direct bond, R_5 being a (C_1-C_3) alkyl; a (C_3-C_{12}) cycloalkyl which is unsubstituted or substituted by a (C_1-C_5) alkyl; a phenyl (C_1-C_3) alkyl which is unsubstituted or substituted by a halogen or by a (C_1-C_5) alkyl; a cycloalkyl (C_1-C_3) alkyl in which the cycloalkyl is C_3-C_{12} and is unsubstituted or substituted by a (C_1 -C_5) alkyl; or a 2-norbornylmethyl.



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18. A method of treatment of hepatic diseases according to claim 16 wherein the CB1 receptor antagonist is N-piperidono-3-pyrazolecarboxamide or one of its pharmaceutically acceptable salt.

19. A method of treatment of hepatic diseases according to claim 16 wherein the CB1 receptor antagonist is N-piperidino-5-(4-bromophenyl)-1-(2,4-dichlorophenyl)-4-ethylpyrazole-3-carboxamide or one of its pharmaceutically acceptable salt.

20. A method of treatment of hepatic diseases according to claim 16 wherein the CB1 receptor antagonist is N-piperidino-5-(4-chlorophenyl)-1-(2, 4-dichlorophenyl)-4-methylpyrazole-3- carboxamide or one of its pharmaceutically acceptable salt.

21. A method of treatment of hepatic diseases according to claims 16 to 20 wherein the hepatic disease is alcoholic liver cirrhosis.

22. A method of treatment of hepatic diseases according to claims 16 to 20 wherein the hepatic disease is chronic viral hepatitis.

23. A method of treatment of hepatic diseases according to claims 16 to 20 wherein the hepatic disease is non-alcoholic steatohepatitis.

24. A method of treatment of hepatic diseases according to claims 16 to 20 wherein the hepatic disease is primary liver cancer.

25. A method of treatment of hepatic diseases according to claims 16 to 24 wherein the daily dosage of CB1 receptor antagonist is from 0.01mg to 500mg, preferably from 1 mg to 100 mg.